Bundesamt für
Verbraucherschutz und
Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Fenflor 300mg/ml Solution for Injection for Pigs

Date: 17 April 2018

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0195/001/MR
Name, strength and pharmaceutical form	Fenflor 300mg/ml Solution for Injection for Pigs
Applicant	KRKA d.d. NOVO mesto Smarjeska cesta 6 SLO-8501 NOVO MESTO Slovenia
Active substance(s)	Florfenicol
ATC Vetcode	QJ01BA90
Target species	Pigs
Indication for use	Treatment of acute outbreaks of respiratory disease caused by strains of *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* susceptible to florfenicol.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	28 May 2018
Date product first authorised in the Reference Member State UK (MRP only)	04 July 2007
Concerned Member States for original procedure	Austria, Belgium, Denmark, Finland, France, Ireland, Italy, The Netherlands, Poland, Portugal, Spain, United Kingdom (former RMS)

I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market. It has been shown that the product can be safely used in the target species; the slight reactions observed are indicated in the SPC. The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy of the product was demonstrated according to the claims made in the SPC. The overall risk/benefit analysis is in favour of granting a marketing authorisation

II. QUALITY ASPECTS

A. Composition

The product contains the active substance florfenicol and excipients dimethyl sulfoxide, propylene glycol and polyethylene glycol 400.

The container/closure system comprises amber Type I neutral glass vials of nominal capacity 50, 100 and 250 ml, closed with bromobutyl rubber bungs secured with an aluminium collar. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and absence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is florfenicol and data have been provided in the form of a European Drug Master File (EDMF). It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitably justified.

All the excipients are the subject of monographs in the European Pharmacopoeia and are provided to that standard.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

E. Control on intermediate products

There are no intermediate products.

F. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.

Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

G. Stability

Stability data on the active substance was discussed in the ASMF in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the finished product when stored under the approved conditions.

An in-use stability of 28 days is supported.

H. Genetically Modified Organisms
Not applicable.

J. Other Information
Shelf life
Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: 28 days.

Special precautions for storage
This veterinary medicinal product does not require any special storage conditions.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies
As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological tests are not required.

The pharmacological aspects of this product are identical to the reference product.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

Toxicological Studies
As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological tests are not required.

The toxicological aspects of this product are identical to the reference product.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

User Safety
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. These are the same as the reference product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

Residue depletion studies using the product were conducted in pigs. Samples of tissues were taken from animals at several time points. After 4 days withdrawal period, all core injection site samples had residues above the muscle MRL but residues were below the LOQ[1] from 8 days onwards. Residues in all other tissues including the surrounding injection sites were below their respective MRLs at all time points.

MRLs

Florfenicol is listed in Annex I of Council Regulation 2377/90. The marker substance is the sum of florfenicol and its metabolites measured as florfenicol-amine.

Pigs	**MRLs**	**LOQ**
Muscle	300 µg/kg	150 µg/kg
Liver	2000 µg/kg	1000 µg/kg
Kidney	500 µg/kg	250 µg/kg
Fat / skin	500 µg/kg	250 µg/kg

Withdrawal Periods

Based on the data provided above, a withdrawal period of 18 days for meat in pigs is justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, pharmacological studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

[1] LOQ = Limit of Quantification, which is the concentration the analytical method can measure with acceptable level of accuracy and precision.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, target species tolerance studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

The applicant has however provided some local target species tolerance studies. The local tolerance of the test product was compared to that of the reference product. No injection site reactions were observed during the study, but mild irritation was noted on histopathology of injection sites during the local tolerance study. No systemic effects were seen, therefore, the local and systemic warnings included in the SPC for Fenflor 300 mg/ml Solution for Injection for Pigs are the same as those for the reference product.

Resistance

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, resistance studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, clinical studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

•	17 April 2018	Change in RMS from UK to DE.
•	05 April 2018	Change to the quality control testing arrangements for the active substance - addition of a site where batch control takes place. Change to the quality control testing arrangements for the active substance - addition of a site where batch control takes place.
•	08 July 2015	Approval of mock-ups.
•	26 March 2015	Removal of distributor.
•	15 March 2013	Change to increase the shelf life of the finished product from 2 years to 3 years.
•	03 February 2012	To add a new supplier for rubber stopper.
•	03 September 2010	New MA – Extension to add a new route of administration (subcutaneous route).
•	02 June 2010	To add a distributor.
•	29 September 2009	New MA (MRP).
•	14 August 2007	Change of Marketing Authorisation Holder.